A STUDY OF QUALITY OF LIFE IN

CHILDREN WITH CANCER

IN HOSPITAL UNIVERSITI SAINS MALAYSIA,

KELANTAN,

MALAYSIA

by

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Dissertation Submitted In Partial Fulfilment of The Requirement for The Degree of Master of Medicine

(Paediatrics)



UNIVERSITI SAINS MALAYSIA

UNIVERSITI SAINS MALAYSIA 2012

ACKNOWLEDGEMENTS

I would like to express my special thanks and deepest gratitude to my dissertation supervisor, Associate Professor Dr. Ariffin Nasir and my dissertation co-supervisor and my personal supervisor, Dr. Norsarwany Mohamad for their continuous guidance, criticism, encouragement and invaluable help throughout the preparation of this dissertation.

My appreciation also goes to the Head of Department of Paediatrics, Professor Dr. Hans Van Rostenberghe Luc Aster for his guidance and encouragement to carry out this study in Hospital Universiti Sains Malaysia. My special thanks also to Dr. Noorizan Abdul Majid, Col. Dr. Wan Pauzi Wan Ibrahim and Dr. Sarimah Abdullah for their guidance in the statistical analysis and my writing.

Also thanks to all my lecturers and my colleagues in the Paediatric Department.

To all my consultants, specialists and colleagues in Pediatric Institute, Hospital Kuala Lumpur, for all their kindness.

To all staff from Pediatric Oncology (ward 6 Utara), the Pediatric Clinic and other oncology wards and clinics (Medical, Ophthalmology, Radiotherapy and Orthopedic) in Hospital Universiti Sains Malaysia

To my beloved parents, my sisters, my brothers and my brothers in law for their everlasting love, support and prayers.

Lastly, to all mothers and children involved in this study, for without them this study would be impossible.

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ABBREVIATIONS

AAP	American Academy of Pediatrics
CPC	Clinical Practise Guidelines
CRHD	Chronic Rheumatic Heart Disease
DM	Diabetes Mellitus
df	Degrees of Freedom
HRQOL	Health Related Quality of Life
HUSM	Hospital Universiti Sains Malaysia
ICC	Intra-class correlation coefficient
MOSTI	Ministry of Science, Technology & Innovation, Malaysia
N	Number of participants
NA	Not applicable
QOLCC	Quality of Life in Childhood Cancer
PCQL-32	Pediatric Cancer Quality of Life Inventory -32
PedsQL TM	Pediatric Quality of Life Inventory TM
SD	Standard Deviation
SLE	Systemic Lupus Erythematosus
SPSS	Statistical Package for Social Sciences
TNO-AZL	Netherlands Organisation for Applied Scientific Research Academic Medical
	Centre
WHO	World Health Organization

DEFINITIONS

Health:

World health organization defined health as 'the complete state of physical, mental and social well being and not merely physical, mental, and social dimensions'

Health-related Quality of Life (HRQOL):

Spieth and Harris defined as the subjective and objective impact of dysfunction associated with an illness or injury, medical treatment, and health care policy.

According to Dr. James, HRQOL is define as the impact of disease and treatment on the patient's self-perceptions of functioning in a variety of domains.

Neutropenia:

An abnormally low level of neutrophils in the blood. Neutrophils are white blood cells (WBCs) produced in the bone marrow that ingested bacteria.

ABSTRAK

PENGENALAN

Pendekatan holistic bukan sahaja melibatkan mengoptimakan rawatan anti-kanser tetapi juga meningkatkan Kualiti Kesihatan Berkaitan Kehidupan (KKBK). Modul PedsQL[™] Kanser 3.0 adalah soal selidik yang telah digunakan secara meluas dan telah disahkan mengikut perkembangan kanak-kanak berumur antara 2 hingga 18 tahun. Ini adalah laporan terulung yang menilai KKBK kanak-kanak kanser dan proksi menggunakan soalan soal selidik kanser spesifik mengikut perkembangan kanak-kanak di Malaysia.

KAEDAH

Para peserta adalah kanak-kanak dan penjaga mereka dengan pelbagai jenis kanser yang menerima rawatan di Hospital Universiti Sains Malaysia (HUSM). PedsQL terdiri daripada 2 set soal selidik, iaitu laporan kendiri kualiti hidup kanak-kanak untuk kanak-kanak berusia 5-12 tahun dan laporan ibu bapa atau proksi QOL kanak-kanak tersebut.

Modul PedsQL[™] Kanser melalui proses linguistik dan kesesuaian budaya ke dalam versi Melayu seperti yang disyorkan oleh Institut Penyelidikan MAPI. Pengesahan lingusitic termasuk penterjemahan ke hadapan dan ke belakang, pengesahan kandungan dan isi dan ujian keboleh percayaan. Keboleh percayaan ditentukan oleh ketekalan dalaman menggunakan 'Cronbach alpha' dan ujian kebolehpercayaan menggunakan Kecekapan Pekali Intra kelas. Versi PedsQLTM 3,0 Kanser Modul (Melayu) yang telah disahkan ini digunapakai kepada kepada 107 kanak-kanak mengidap kanser (bagi yang berumur 5 hingga 18 tahun) dan 137 proksi ibu bapa (bagi yang berumur 2 hingga 18 tahun) di HUSM, Kelantan, Malaysia. Ujian berpasang -t telah digunakan untuk menentukan perbezaan min di antara skor KKBK kanak-kanak dan proksi ibu bapa (kecuali untuk kumpulan umur 2 hingga.

Multifaktorial	ANOVA	telah	digunakan	untuk	membandingkan	skor	min	KKBK	antara
kumpulan	(dala	m	rawat	tan	dan	tam	at	ra	watan).

KEPUTUSAN

Pekali alpha Cronbach adalah antara 0.77 hingga 0.93 untuk kanak-kanak dan 0.80 hingga 0.93 untuk laporan proksi ibu bapa. Pekali korelasi Intra kelas adalah di antara 0.88 hingga 0.92 untuk kanak- laporan kanak dan 0.86 hingga 0.91 untuk laporan proksi ibu bapa. Skor laporan proksi ibu bapa jauh lebih rendah secara signifikannya berbanding dengan kanak-kanak di seluruh semua peringkat umur [68.9 (19,20) vs 73.4 (18.8)]. Domain 'Kebimbangan Prosedur' didapati terletak di bawah aras titik penentu yang menunjukkan risiko KKBK yang terjejas (min kurang daripada 70) merentasi semua kumpulan umur (antara 39 hingga 65.9). Selepas diselaraskan untuk jantina dan diagnosa, skor KKBK untuk kumpulan 'dalam rawatan' jauh lebih rendah daripada kumpulan 'rawatan selesai' merentasi sebahagian besar daripada kumpulan umur (kecuali laporan proksi ibubapa untuk 2-4 dan 8-12).

KESIMPULAN

Modul PedsQL Kanser 3.0 (versi Melayu) linguistik disahkan dan setanding dengan soal selidik asal dan lain-lain yang diterjemahkan. Ujian soal selidik untuk kanak-kanak dengan kanser dan proksi mereka mendedahkan laporan proksi ibu bapa cenderung untuk memandang rendah KKBK kanak-kanak. Kebimbangan prosedur telah dikenalpasti sebagai domain utama KKBK yang terlibat dalam anak-anak kita. Secara amnya, KKBK kanak-kanak dalam rawatan terjejas tetapi bebas dari kebergantungan kepada jantina atau diagnosa, berbanding dengan kanak-kanak yang telah selesai rawatan.

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KATA KUNCI:

Kualiti Kesihatan Berkaitan Kehidupan, Kanser Pediatrik, Validasi versi terjemahan bahasa Melayu soal-selidik PedsQLTM Module Kanser 3.0.

.

ABSTRACT

Background

Holistic approach not only involve optimizing anti-cancer treatment but also improving Health Related Quality of Life. PedsQLTM Cancer Module is a widely used validated and developmentally appropriate questionnaire designed to measure pediatric cancer specific HRQOL for children age 2 to 18 years. This is the first report validating and assessing children and also first proxy report in HRQOL of children treated for cancer using cancerspecific and developmentally-appropriate questionnaire for children in Malaysia.

Methods

The participants were children and their caretakers with various types of cancers who received treatment in Hospital Universiti Sains Malaysia (HUSM). The PedsQL consists of 2 sets of questionnaires, which are pediatric quality of life self-report for children ages 5-12 years and parent-proxy report of child QOL questionnaire.

PedsQLTM Cancer Module was culturally and linguistically validated into Malay version as recommended by MAPI Research Institute. Lingusitic validation included forward and backward translation, face and content validation and reliability test. Reliability was determined by internal consistency using Cronbach alpha and test-retest reliability using Intra-class Coefficient Efficiency. The validated Malay version PedsQLTM 3.0 Cancer Module (Malay) was administered to 107 children with cancer (for aged 5 to 18 years) and 137 parental proxies (for aged 2 to 18 years) in HUSM, Kelantan, Malaysia. Paired t-test was used to determine the mean difference between child and parental proxy HRQOL scores

(except for age group 2 to 4). Multifactorial ANOVA was used to compare the mean scores of HRQOL between groups (on treatment versus completed treatment).

RESULTS

Cronbach's alpha coefficients ranged from 0.77 to 0.93 for children and 0.80 to 0.93 for parental proxy reports. The Intra-class correlation coefficient was between 0.88 to 0.92 for children reports and 0.86 to 0.91 for parental proxy reports. The parental-proxy HRQOL reports scored significantly lower compared to children across all age groups [68.9 (19.20) vs 73.4 (18.8)]. The mean cut-off point for domain at risk of impaired HRQOL (less than 70) was 'Procedural Anxiety' across all age groups (between 39 to 65.9). After adjusted for gender and diagnoses, there was also significantly lower HRQOL score between 'on-treatment' and 'completed treatment' group across most of the age groups (except parental proxy reports for 2-4 and 8-12).

CONCLUSION

PedsQL 3.0 Cancer module (Malay version) was linguistically validated and comparable to original and other translated questionnaire. Administration of the questionnaire to children with cancer and their proxy revealed that parental proxy reports tend to underestimate the HRQOL of children. "Procedural Anxiety" was identified as the main HRQOL affected subscale in our children. Children on treatment generally had impaired HRQOL independent of gender and diagnoses.

KEYWORDS:

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Health Related Quality Of Life, Pediatric Cancer, Validated Malay version PedsQLTM Cancer Module 3.0 Questionnaires.

A STUDY OF QUALITY OF LIFE OF CHILDREN WITH CANCER IN HOSPITAL UNIVERSITI SAINS MALAYSIA, KELANTAN,

MALAYSIA

1 INTRODUCTION

In Malaysia, there are a few Pediatric Oncology tertiary centers distributed in different states. Hospital Universiti Sains Malaysia (HUSM) is one of the tertiary centre in Malaysia and it covers East-coast of Peninsular Malaysia, which includes Kelantan, Terengganu and Pahang.

1.1 Epidemiology

Pediatric cancer was once regarded as a fatal illness. Currently it is considered as lifethreatening, chronic disease in the majority of cases (Bradlyn et al., 1993, Ekert, 1989, Koocher, 1981), with extended periods of remission and prolonged survival.

For children with cancer, long-term survival and cure is expected depends on type of cancer and stage of disease at diagnoses (Ekert, 1989, Koocher, 1981). Aggressive medical treatments have offered a new hope for cure and prolonging their survival to a greater number of children with cancer.

Due to dramatic improvement in the survival of the children with cancer, the quality of life (QOL) during and following treatment has emerged as an important health outcome. The quality of life should measure numerous short term and lasting undesirable somatic, psychological, neuropsychological, educational and / or psychosocial sequelae (Jenney et al., 1995, Gamis and Nesbit, 1991, Peckham, 1991, Anderson et al., 1994, Adams and Deveau, 1988, Mulhern et al., 1990).

A reliable and valid QOL measurement instrument is needed. This measurement is useful to assist individual families of the children with cancer, in making treatment decisions and predict future psychological or behavioral outcomes. It also can be used in clinical trials or decision analyses to calculate quality-adjusted life years.

So far in Malaysia, there was only one formal study done on Quality of Life in Children with Cancer in Malaysia for Acute Lymphoblastic Leukemia patients (Hamidah et al., 2011). This study is the first to analyze the Quality of Life in Children with Cancer in HUSM, Kelantan, Malaysia.

1.2 History

World Health Organization defined health as 'the complete state of physical, mental and social well being and not merely physical, mental, and social dimensions' (WHO, 1947). Child health has been defined as the ability to participate fully in developmentally-appropriate activities and requires physical, psychological, and social energy (Pantell and Lewis, 1987).

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There is a difference within health and quality of life. Most current attempts to define QOL in pediatric oncology settings have been guided by the WHO criteria and adult oncology studies (Aaronson, 1991, Spieth and Harris, 1996). Spieth and Harris defined Health-related Quality of Life (HRQOL) as 'the subjective and objective impact of dysfunction associated with an illness or injury, medical treatment, and health care policy'. (Spieth and Harris, 1996)

However, there were controversies in defining and assessing QOL, which have not been resolved until now. Varni et al defined HRQOL as the impact of disease and treatment on the patient's self-perceptions of functioning in a variety of domains (Varni et al., 1998a).

In pediatric settings, health-related quality of life (HRQOL) continues to grow in importance as an outcome measure, especially in the pediatric cancer population. The evaluation of the impact of treatment and its associated late effects on quality of life has become important (Shankar et al., 2005, Feeny et al., 1999, Levi et al., 2001, Cullen and Stenning, 2004).

1.3 Quality of life

Children with cancer are at risk of problems in physical, psychological, social, growth and education achievements. The diagnosis and treatment of childhood cancer can be a traumatic experience for patients and their families. Traditionally, the approach to improve health-related quality of life (HRQOL) is emphasized on intensive mode of treatment rather than improving aspects of social, psychological and physical aspect of quality of life (Varni et al., 2007).

With the treatment using both chemotherapy and radiotherapy, the life expectancy has improved, but they may have their adverse effects that may manifest later in life. In addition to the development of malignancy, patients are at risk of growth and endocrine dysfunction, infertility and many other organ dysfunctions (Langeveld et al., 2004). Stevens et al. (1998) found that more than half of the survivors of childhood cancer had at least one chronic medical problem.

In the current literature, the five core domains in QOL measures can be expanded into: (1) Disease state and symptoms, (2) Physical functional status, (3) Psychological functioning, (4) Social functioning (Aaronson, 1988) and (5) Cognitive functioning (Varni et al., 1998b).

Assessment of QOL of children is more complex due to several conceptual and methodological issues (Landgraf et al., 1999). The complexity of assessing QOL is due to the developmental differences in understanding the content measured. The underdevelopment of QOL concept for pediatric cancer patients may result in false conclusions, and subsequently, improper clinical intervention (Hinds and Haase, 1998).

Since the assessment of QOL depends on one's subjective judgment, it would be inappropriate to assess QOL without considering one's perception regarding the understanding of their status. Measures of HRQOL in children may use either self-report or proxy report (Russell et al., 2006). Proxy reporters most often are parents, but occasionally others such as grandparents or relatives.

There are many reasons for the use of parental or other proxy reports for the assessment of children's HRQOL, including cases in which the child may be too young or too ill to accurately report on their HRQOL (Levi and Drotar, 1999).

1.4 Concerns of children with cancer

Although the aggressive treatment protocols in pediatric oncology may be successful in curing most of the children with cancers and prolonging life in others, but it too has major effects on their lives. Some of these lifestyles changes include home schooling, hospitalization, and frequent clinic visits for infusions of medications, blood products and regular clinic follow up.

The general psychological effects of cancer on long-term survivors have been studied. The effects on the lifestyle changes in cancer children actively receiving therapy are still largely unknown (Zebrack and Chesler, 2002).

These effects of lifestyle changes with the aggressive treatments such as hospitalization, home schooling or missing schooling for patients have become one of the concerns on the quality of life for the children with cancer. Moody et al in 2006, concluded four major concerns of children with cancer which include (Moody et al., 2006):

- (1) Loneliness, isolation, and loss of a normal childhood activity
- (2) Decreased pleasure from food
- (3) Physical discomfort and disability
- (4) Emotional responses to cancer specifically anger and fear.

1.4.1 Loneliness, isolated and loss of a normal childhood activity

Children with cancer usually feel lonely, isolated and loss of normal childhood compared to other healthy children. They would like to be able to have a more normal childhood as other healthy children do. That would be having a peer group and engaging in a normal childhood activities such as going to school, make new friends, hang out at the mall, participating in sports and graduate with their peers. However, with their disability, frequent hospital visits and admissions, they are unable to do so. Many of the children with cancer even felt inferior than their peers as their schoolwork have fallen behind, and they would not be able to go to college with their peers (Woodgate, 2000b, Woodgate, 2000a).

Children with cancer also reported that they do not have any friends in hospital. In the hospital, even though they had arranged group activities in the playroom for hospitalized children, the children with cancer were rarely expose to other children with their age. Furthermore, due to their severe neutropenia, many of these children were on isolation precautions and could not go to the playroom with the others, even at home.

Ultimately, these children became disconnected from the other, which leads to their feelings of isolation and loneliness. Some of the children had reported that they felt some of the friends were uncomfortable being around them. Those friends who kept in contact with them, and had visited them in the hospital after their diagnosis of cancer were their "real friends".

1.4.2 Decreased pleasure from food

The children were unable to enjoy their food as their poor appetites, changes in taste and smell sensations, emetogenic chemotherapy, and restrictions in food choices.

In addition to the dislike of the hospital food, they had restricted food choices. These restrictions varied significantly and ranged from the elimination of processed sugar to the elimination of fresh vegetables. Some of the food restrictions were suggested by the medical staffs to reduce the risk of infection from the food during the periods of neutropenia, or contraindication for the chemotherapy during their chemotherapy treatment. Restrictions also sometime were imposed by the parents because of beliefs they had about cancer and diet (Enskar et al., 1997b).

1.4.3 Physical discomfort and disability

Nausea is the most frequent form of physical discomfort for the children during and after their chemotherapy or radiotherapy. The bad taste with the medicine may even cause more disability and discomforts by making them feel nauseated.

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Pain is another major complaint, which mostly caused by needle sticks or disease itself. Despite the usage of local or systemic analgesic, and long term central line, pain was still a traumatic event for them. This traumatic event may even be follow by nightmare throughout all their lifetime, even after they had completed their treatment.

The limitation of physical function was another significant issue for them, as it may be a permanent change for them. They can be easily fatigued than before, which pertained to disability and discomfort. They may even have psychological deficit (Enskar et al., 1997a, Hockenberry-Eaton et al., 1998).

1.4.4 Emotional responses to cancer specifically anger and fear

The children with cancer may express their stress of living with cancer in different ways. They can feel angry about having cancer, fear over the sickness and time of their life with their cancer, concerned over the death and their potential death would affect their parents or others.

Some children have the feeling of vulnerability over the thought of whether they will survive or die every night. Some of them would be worried over the persistent or relapse of their cancer, while during the treatment or frequent follow up. They even worry about whether they are a burden to their family or others (Hockenberry-Eaton and Minick, 1994).

1.5 Consequences of cancer to the adolescence

In this century, children with cancer have better survival rate, but in exchange of their long-term physical, psycho-social distress and as well as positive experiences (Good self esteem, knowledge and experience with regard to disease and hospital care. Good relations, broader perspectives and material gains.) (Barakat et al., 2006, Richardson et al., 1999, Stam et al., 2006, Stuber et al., 1997). Some of the long-term physical distresses include amputation or deformities of limbs, overweight, different size and shape of scars, loss of muscles, change in their hair colours and quality, problems with coordination, as well as being too short from the other healthy children (Novakovic et al., 1996).

1.6 Concerns of family and patient after treatment

Many studies had been highlighted several difficulties for some survivors been in adult life. These include problems with schooling and employment, insurability, the ability to marry and have children, and in establishing stable relationships with family and friends (Evans and Radford, 1995, Haupt *et al.*, 1994, Hays *et al.*, 1992, Kelaghan *et al.*, 1988, Langeveld *et al.*, 2003, Rauck *et al.*, 1999, Byrne *et al.*, 1989, Zeltzer, 1993)

Few studies had systematically investigated on self-esteem and self-reported concerns and fears in young adult survivors (Coopersmith, 1981, Shavelson and Bolus, 1982).

The potential psychosocial problems for survivors such as problems with schooling and employment, insurance denial, difficulties in forming relationships and adverse changes in appearance, can result in a possible lack of self-esteem (Evans and Radford, 1995). In several studies childhood cancer survivors reported worries about cancer-specific issues and general health issues even many years beyond the end of their treatment (Wasserman et al., 1987; Smith et al., 1991; Gray et al., 1992; Haase and Rostad, 1994; Weigers et al., 1998).

It would be useful to predict who is most likely to worry, in order to direct possible resources for psychological help. As noted by Weigers et al. (1998), understanding the worries of long-term survivors may be important for two reasons. First, degree of worry, or anxiety, had been shown to be an important component of overall adjustment (Holland and Rowland, 1990). Second, the self-reported worries of survivors may provide a starting point for the development of effective long-term support for them.

The success on survival in children treated for malignancies has led to shifts in parental worries. Survival was formerly the primary point of concern; with currently late effects are importance issues as well. Fertility is one of these points. In the literature, many studies on assumptions on cancer survivor fertility and their psychosocial consequences were publishing. In the case of a child with cancer, parents are often the cornerstones with respect to collection of information. In fact, they are leading actors in provision of information to their child.

1.7 Questionnaires for Children with Cancer Module

There are many studies of HRQOL in Pediatric cancer patients using different questionnaires, examples include:

- PCQL-32: Pediatric Cancer Quality of Life Inventory -32 (Varni et al., 1998a)
- PedsQL[™] Cancer module version 3.0 for the children with cancer by Dr James W.
 Varni (Varni et al., 2001)
- PedsQLTM 4.0 Generic Core Scales by Dr James W. Varni (Varni et al., 2002b)
- TNO-AZL (Netherlands Organisation for Applied Scientific Research Academic Medical Centre) Questionnaire for Children's Health Related Quality of Life (Knoester et al., 2008)
- KIDSCREEN instruments are a family of generic quality of life measures that have been designed and normed for children and adolescent aged between 8 to 18 years (Hong et al., 2007, Ravens-Sieberer et al., 2005, Ravens-Sieberer et al., 2008)
- QOLCC: Quality of Life in Childhood Cancer instrument for measuring the quality of life of Taiwanese children with cancer (Yeh et al., 2004a, Yeh and Hung, 2003, Yeh et al., 2004b)
- RAND Health Insurance Study (Alman et al., 1996)
- Child Health and Illness Profile (Estrada et al., 2010, Rajmil et al., 2004, Gerson et al., 2005)

PedsQL questionnaires has both generic core scales and various disease-specific questionnaire for many chronic diseases. PedsQL Generic Core questionnaire developed

by Dr James Varni, known as PedsQL 4.0 was the result of extensive iterative process over the past 25 years. PedsQL 4.0 Generic Core Scales questionnaire has been translated into more than 65 languages with international data of more than 35,000 healthy children and children with chronic conditions and published in more than 345 peer reviewed journals (Varni and Limbers, 2009).

Based on this Generic Questionnaire, many diseases and chronic conditions questionnaires were developed. These include PedsQL Asthma (Varni et al., 2004), Arthritis/Rheumatology (Varni et al., 2002c), Brain Tumour (Palmer et al., 2007), Cardiac (Uzarka et al., 2003), Cerebral Palsy (Chan et al., 2005), End Stage Renal Disease, Diabetes (Varni et al., 2003a) and many others including PedsQL 3.0 Cancer Module.

PedsQL 3.0 Cancer Module was designed to measure pediatric cancer specific HRQOL (Varni et al., 2002a)

Similar to the Generic Core questionnaire, it also has been validated and used widely on Pediatric Oncology patients (Lau et al., 2009, Scarpelli et al., 2008, Sitaresmi et al., 2008, Tsuji et al., 2011, Varni et al., 2002a). The questionnaire contains 27-item with eight domains with parallel child self report and parental proxy report formats, exactly like PedsQL 4.0. This format enables one to compare reports between parents and child and between healthy and other chronic conditions but at the same time it is disease-specific. For these reasons, we have chosen PedsQL 3.0 Cancer Module as the questionnaire for our study.

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2 OBJECTIVE

2.1 General objective

To determine the child and parent proxy-report health related quality of life (HRQOL) using the PedsQLTM 3.0 Cancer module Questionnaire in children with cancer in Hospital Universiti Sains Malaysia.

2.2 Specific objective

2.2.1 Phase I Study

To validate the English version of PedsQLTM 3.0 cancer module questionnaire to Malay version PedsQLTM 3.0 cancer module.

2.2.2 Phase II Study

- To determine mean difference of child's HRQOL scores and parental proxy HRQOL scores using validated Malay version PedsQLTM 3.0 cancer module.
- To compare the child's HRQOL scores between children on treatment and those who had completed treatment using validated Malay version PedsQLTM 3.0 cancer module.
- To compare the parental proxy HRQOL scores between children on treatment and those who had completed treatment using validated Malay version PedsQLTM 3.0 cancer module.

3 HYPOTHESIS

- The Malay version of PedsQLTM 3.0 cancer module is reliable and valid as compared to other translated versions.
- There is a difference in total mean score of HRQOL between child and parental proxy scores using Malay version PedsQLTM 3.0 cancer module.
- There is a difference in total mean score of HRQOL between children on treatment and those completed treatment using Malay version PedsQLTM 3.0 cancer module.
- There is a difference in total mean score of parental proxy HRQOL between children on treatment and those completed treatment using Malay version PedsQLTM 3.0 cancer module.

4 METHODOLOGY

4.1 Study setting and participants

This study was done from April 2008 until June 2009. It was conducted in Hospital University Sains Malaysia (HUSM), which is a regional center for childhood malignancies in East Cost of Malaysia.

In this study, there were two groups of participants, children with cancers and their parents or guardians. Participants were stratified according to children's age and treatment completion. The treatment groups were "on treatment" and "completed treatment".

Children with cancers were identified from admission registrations in HUSM. They were from Pediatric, Medical, Ophthalmology, Radiotherapy and Orthopedic wards and clinics.

Children with cancers

On-treatment status was defined as children with cancers who were receiving therapy for their cancers included newly diagnosed or recurrent disease. Completed-treatment status represented children with cancers whom had completed all therapy at the time of assessment. (Varni et al., 2002a).

Parent or guardian of children with cancer

Parent or guardian of children with cancers at the age of 2 to 18 years old, whom had participated in this study along with their child.

Inclusion criteria:

Participants were Malay children with cancer between 2 to 18 years old who consented and admitted or come for follow up to the oncology wards or clinics and their parents or guardians.

Exclusion criteria:

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Exclusion criteria were children with known congenital anomalies or syndrome or multiple major disorders (e.g CRHD, DM, SLE etc).

4.2 Instrument

The original research instrument used in this study was a validated English version Pediatric Quality of Life Inventory (PedsQL)TM, Cancer Module, version 3.0 questionnaires, which was developed and validated by Dr James W. Varni (http://www.mapi-trust.org/questionnaires/50). Permission to use the questionnaire was obtained from MAPI Research Institute, Lyon, France. (Appendix 11.1)

PedsQLTM Cancer Module 3.0 consists of developmentally-appropriate forms for children with cancers according to the child's age groups: 2 to 4 years old (parent), 5 to 7 years old (child and parent), 8 to 12 years old (child and parent) and 13 to 18 years old (child and parent).

The English version questionnaire was translated and validated into a Malay version. The Malay version questionnaire was then applied to children with cancers and / or their parents or guardians. Children ages 5 to 18 years completed the child self-report and parents or guardians of children ages 2-18 years would complete the parent proxy-report.

The questionnaire consists of developmentally appropriate forms according to the age groups (2 to 4, 5 to 7, 8 to 12, 13 to 18). All sub group questionnaires contained eight domains and consisted of similar number of items for all age groups, except for cognitive domain:

- Pain and hurt (2 items),
- Nausea (5 items),

- Procedural anxiety (3 items),
- Treatment anxiety (3 items),
- Worry (3 items),
- Cognitive problems (3 items for child ages 2-4, 4 items for child ages 5-7, 5 items for child ages 8-12 and teen ages 13-18),
- Perceived physical appearance (3 items)
- Communication (3 items).

Likert Scales:

A 5-Likert Scales response scale is utilized across child self-report for ages 8–18 years and parent proxy-report (0 = never a problem; 1 = almost never a problem; 2 =sometimes a problem; 3 = often a problem; 4 = almost always a problem).

To further increase the ease of use for the young child self-report (ages 5 to 7 years), the Likert scale is reworded and simplified to a 3-point scale (0 = not at all a problem; 2 = sometimes a problem; 4 = a lot of a problem), with each response choice anchored to a happy to sad faces scale ($\bigcirc = 0$; $\bigcirc = 2$; $\bigotimes = 4$).

Parent proxy-report also includes the toddler age range (ages 2 to 4 years), which does not include a self-report form given developmental limitations on self-report for children younger than 5 years of age.

Items are reverse-scored and linearly transformed to a 0 - 100 scale as: 0 = 100, 1 = 75, 2 = 50, 3 = 25 and 4 = 0. The highest scores indicate better HRQOL.

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The questionnaire was interviewer-administered for children aged 5 to 7 years by the author, and self administered for children ages 8 to 18 years. A standardized case recording form was used to record the demographic and socioeconomic data. (Appendix 11.4)

4.3 Study design

This study consisted 2 phases: phase I and phase II. The flow chart for the whole study was outlined in Figure 1.



Figure 1: Flow chart for the whole study

4.3.1. Phase I Study: Validation of PedsQL version 3.0 Cancer English module questionnaires into Malay language

In this phase, linguistic validation of the PedsQL was developed in close collaboration with MAPI Research Institute in Lyon, France and with Dr James W. Varni (<u>www.pedsql.org/PedsQL-Linguistic-Validation-Guidelines.doc</u>). The aim of the linguistic validation was to produce a Malay version of PedQLTM 3.0 Cancer module from original English version.

Linguistic validation of a QOL questionnaire:

The linguistic validation consisted of four steps:

- Forward translation
- Backward translation
- Face and content validation
- Reliability of the questionnaires

Forward translation step

One local professional translator (from language centre HUSM) and four Pediatricians translated the original English version. Each of the translators independently produced a forward translation of the original items, instructions and response choices (Forward translation versions). The translated versions were discussed and agreed on to a single reconciled version (PedsQL Malay version 1.0) by expert panel members. The expert panel members consisted of two Pediatric Oncologists, two Pediatricians, two Psychiatrists, one Psychologist and a Biostatistician. A written report then was sent to Dr James W. Varni for verification of the procedure.

Backward translation step

Another professional bilingual translator and three Pediatricians translated PedsQL Malay version 1.0 back into English language. The expert panel then compared the backward translated versions with the original English version. This discussion resulted in PedsQL Malay version 2.0. Second written report was sent to Dr James W. Varni for verification of the procedure.

Face and content validation

The PedsQL Malay version 2.0 was tested on 20 participants using child self report forms and parental proxy report forms for face and content validation. There were five pairs of participants (child and their parent or guardian) from each age group, except for age group 2-4, only the parent or guardian took part. Both the children and their parents or guardians were interviewed for understanding and identification of any problems with the questionnaires. The interviewed took place separately. A series of amendments to PedsQL Malay version 2.0 by expert panel members resulted in PedsQL Malay version 3.0. This version was taken as the final version. A third written report was sent to Dr James W. Varni for verification of the procedure.

Reliability of the questionnaires

The PedsQL Malay version 3.0 was then applied to the target population consisted of 24 participants (children with cancers and their parent or guardian). The same 24 patients were retested after one week. Cronbach's Alpha Coefficients and Intra-class correlation coefficient (ICC) were calculated.

If the Internal Consistency by Cronbach's alpha coefficients at the end of the study was > 0.7, then the PedsQL Malay version 3.0 was considered validated for the Phase II study. (*Scientific Advisory Committee of the Medical Outcomes Trust. QOL Res 2002, 11:193 - 205*). If the Cronbach's alpha was < 0.7, then a second group of participants would be tested. If the result remained < 0.7, then the whole process would need to be repeated.

The summarized process for phase I study was shown in Figure 2.



